about the role of "second-look" laparotomy in the management of ovarian carcinoma. Here the sensitivity of the test is only 33%, but the specificity is 100%. The negative predictive value is 57%, and the positive predictive value is 100%. Thus, a second-look laparotomy is unnecessary in a patient with an elevated CA 125 level except in a research setting where the quantification of disease is essential for evaluating experimental protocols.

Several studies have investigated the usefulness of CA 125 levels as a screening test. Evaluating 1,020 female blood donors using a cutoff of 65 U per ml resulted in a 1.8% positive test rate. Of these, 0.7% were pregnant and only 0.3% tested positive at a second screening. Cervical adenocarcinoma, endometrial adenocarcinoma, fallopian tube carcinoma, and nongynecologic cancerous lesions such as those of the pancreas, lung, liver, breast, colon, stomach, and biliary tract have also been associated with elevated CA 125 levels. Yet elevated CA 125 levels do not necessarily imply the presence of malignancy, as elevations have also been seen with benign conditions such as pregnancy, endometriosis, menstruation, pelvic inflammatory disease, pancreatitis, peritonitis, benign ascites, and leiomyomata. Selecting a patient population with a pelvic mass for screening CA 125 levels increases the usefulness of the test. Here the sensitivity is 93% and the specificity is 87%.

In conclusion, CA 125 levels are useful in the management of ovarian carcinoma, as levels correlate with the volume of ovarian cancer present. CA 125 functions as a leading indicator of disease progression but loses considerable sensitivity during the course of disease. Likewise the predictive value of a positive test is excellent, but a decline in the value of a negative test is observed during therapy. The selection of drug-resistant cell lines that have lost the ability to make CA 125 undoubtedly contributes to these results. Further research in the area of tumor markers now focuses on the usefulness of the simultaneous measurement of several markers. It is hoped that such an approach will further facilitate the diagnosis and treatment of ovarian carcinoma.

RICHARD E. BULLER, MD, PhD
PHILIP J. DiSAIA, MD
Irvine, California

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Drug Therapy for Genital Herpes

ACYCLOVIR, a synthetic purine nucleoside analogue, is effective when taken orally or intravenously for primary or recurrent genital herpes. During a one-year treatment trial for frequently recurring genital herpes—that is, six or more recurrences per year—the likelihood of being symptom-free for a year was increased from 2% to 44% and the mean number of recurrences reduced from 11.4 to 1.8. This degree of efficacy has led to longer treatments. But concerns that remain unanswered include the probability of viral resistance developing and increased or additional toxicity. With short-term courses, the most common adverse effects are nausea and vomiting, occurring in about 3% of patients.

The intravenous use of acyclovir requires admitting to hospital and is generally reserved for patients with life-threatening infections. Topical acyclovir is not as effective as oral, has limited efficacy in treating recurrent disease, and has no demonstrated ability to prevent recurrences. For primary genital herpes, administering acyclovir orally, 200 mg five times a day for five to ten days, has been effective in reducing the duration of shedding and severity and duration of symptoms.

Acyclovir prophylaxis—400 mg twice a day—for patients with frequent or severe recurrences has been administered for at least a year in clinical trials. Most cases with acyclovir-resistant organisms have been found in immunocompromised patients. Such resistance has thus far not been associated with progressive disease, and in most instances subsequent recurrences were caused by acyclovir-sensitive organisms. Further studies are required to determine whether long-term suppression reduces or facilitates the emergence of clinically important drug-resistant mutants in this population.

The use of acyclovir in pregnancy, breast-feeding mothers, or newborns has not been shown safe. The Burroughs Wellcome Company has a registry of its use in pregnancy (telephone number [919] 248-4017). No specific adverse effects on mothers or fetuses have been recognized. For women with primary herpes in pregnancy, some authors have recommended using acyclovir because of initial reports of associated preterm labor and slowed intrauterine growth rate. Others, however, would only recommend its use during pregnancy or childhood for life-threatening disease or herpes simplex virus infection of immunocompromised patients. Women with visible genital herpes at the beginning of labor are advised to have delivery by cesarean section to avoid the serious consequences of neonatal herpes. Many cases of neonatal herpes result from genital excretion of herpes simplex virus type 2 by a mother who may never have experienced genital herpes symptoms. Viral cultures before labor do not predict later exposures, but cultures obtained during labor of women with previous genital herpes may be valuable in identifying babies at risk for infection and lead to more timely treatment.

PAUL A. HENSLEIGH, MD, PhD
Santa Clara, California

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β-Streptococcal Cultures in Obstetrics

β-HEMOLYTIC STREPTOCOCCI play a role in two major areas of obstetrics: puerperal fever (primarily group A or *Streptococcus pyogenes*) and antepartum and intrapartum infections (primarily group B or *Streptococcus agalactiae*). All standard antibiotic regimens for the treatment of puerperal fever or postpartum endomyometritis include coverage for group A streptococci, and this organism is no longer responsible for the mortality that it was in the past. Group B streptococci, on the other hand, have recently been recognized as important pathogens in neonatal sepsis and possibly as etiologic agents for preterm premature rupture of the membranes and chorioamnionitis.

About 10% to 30% of pregnant women carry group B streptococci in the birth canal. The rate of carriage seems to be higher in white women younger than 20 years. At birth, approximately 10% to 15% of infants delivered of carrier mothers will become colonized (as opposed to infected) with the organism. The attack rate for true infection, which can result in severe sepsis and a 50% neonatal mortality rate, is about 1 in 1,000 at term but much higher in a preterm infant, women with intrapartum fever, or in premature rupture of the membranes. Thus, the question of how to prevent infection with group B streptococci is difficult to answer and has led to controversy among experts in perinatology and neonatology. If all pregnant women were to be screened and treated to eradicate the infection during pregnancy, such treatment would benefit only the 5% of patients who may experience preterm labor or premature rupture of the membranes and the 1 per 1,000 term infants who will contract group B streptococcal sepsis. This benefit would be at the cost of administering ampicillin to as many as 30% of all pregnant women. Furthermore, many such patients would become recolonized by the reservoir of organisms in the rectum; penicillinase-producing bacteria prevent the eradication of this reservoir. Repeated culturing and retreatment throughout the pregnancy would be necessary. Thus, most experts think that only patients with premature rupture of the membranes, preterm labor, or maternal fever during labor, or patients at risk for such events (twins, triplets, history of premature rupture of the membranes or preterm labor) should be cultured for group B streptococci and treated. For such patients, the best technique is to swab the outer third of the vagina, as this area provides the highest yield of cultures positive for the organism. Those patients with positive cultures and premature rupture of the membranes should be treated with ampicillin given intravenously, 1 gram every six hours, for five days or until delivery; cultures should be repeated every one to two weeks and treatment repeated if recolonization has occurred. Patients with intact membranes may be given oral ampicillin, 500 mg every six hours for five to seven days. For those patients with active labor or prematurely ruptured membranes, an alternate scheme is to treat all on admission until culture results become available. Experts appear to be equally divided concerning the relative risks and benefits of such an approach.

Certain patients should probably be screened and treated throughout the entire period of fetal viability to suppress group B streptococci colonizing the birth canal. This group includes patients with cervical cerclage, those with a previous infant who died of group B streptococcal sepsis, and patients at extremely high risk of preterm labor or premature rupture of the membranes. For this group, prescribing ampicillin, 500 mg by mouth every six hours, from approximately 24 weeks to delivery is appropriate. Penicillin V potassium, while effective against group B streptococci, has not been adequately tested and may allow an overgrowth of gram-negative organisms in the vagina.

At present, then, routine screening of all pregnant women for group B streptococci is not recommended, as most will have a term birth and only 10% to 30% will be colonized at the time of screening; colonization may occur after a negative screen as well. Treatment of sexual partners also is not of benefit, as the major source of recolonization of the birth canal is the reservoir of organisms in the rectum.

If group B streptococci are searched for and eradicated in a patient at high risk for preterm delivery, the severe neonatal consequences of this infection in newborns can be reduced.

R. HAROLD HOLBROOK, JR, MD
Stanford, California

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Estrogen Hormone Replacement to Minimize Cardiovascular Risk

IN THE UNITED STATES, heart disease is the leading cause of death in women. More than half of all women will die of some sort of cardiovascular disorder. The incidence of cardiovascular disease in women is less than that in men until the menopause occurs. After menopause, the cardiovascular disease incidence increases at the same rate as in men so that by the age of 60 it approaches that of men and by the age of 90 the disease is equally present in both sexes.

As shown by the Framingham study and others, the risk for cardiovascular disease is related to a great extent to the level of blood lipids. In particular, high levels of triglycerides, low-density lipoprotein (LDL), and total cholesterol and low levels of high-density lipoprotein (HDL) place one at an increased risk for cardiovascular disease. Currently 50% of women in the United States have a total blood cholesterol level greater than that recommended by the National Institutes of Health. Because a 1% decrease in the cholesterol level produces a 2% decrease in the incidence of coronary artery disease, efforts to reduce blood cholesterol levels are warranted.

Following the menopause, levels of cholesterol and LDL increase and levels of HDL decrease. The replacement of estrogen after either the natural menopause or surgical castration has been shown to prevent these changes and favorably alter the lipid profile in women. Estrogen therapy decreases total cholesterol and LDL levels whereas it increases HDL levels. If the risk reductions associated with these changes in blood lipids are combined, a significant reduction would be expected in the risk of cardiovascular disease with postmenopausal estrogen replacement therapy. Several recent case-control and cohort studies have shown this decreased risk.

There are several estrogen preparations available on the market today. It is difficult to summarize the published data because of the various routes of administration, doses, and preparations used. Nevertheless, trends can be identified. When estrogen is given orally, it lowers cholesterol and LDL levels and raises HDL levels, but it may take up to several months for these beneficial effects to occur. When estrogen is delivered percutaneously, the favorable effects on lipids are reduced.

Because of the risk for endometrial hyperplasia and malignancy, the addition of progestin to estrogen replacement regimens is necessary in women who have a uterus. Unfortunately, the progestins have an effect on blood lipids opposite to that of estrogens and tend to raise cholesterol and LDL levels and lower HDL levels. In studies that have evaluated the combination of estrogen plus progestin, the effect on blood lipids depends to a great extent on the progestin chosen. Specifically, the 19-nortestosterone derivatives of